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Sporadic Creutzfeldt-Jakob Disease After Receiving the Second Dose of Pfizer-BioNTech COVID-19 Vaccine

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Abstract

- Human prion disease is a rare, highly progressive neurodegenerative disease that is ultimately fatal.
- The majority of cases occur sporadically, although some may be genetic or acquired.
- Here, we highlight a case of a 64-year-old woman who presents with rapidly declining memory loss, behavior changes, headaches, and gait disturbance approximately one week following administration of the second dose of the novel Pfizer-BioNTech messenger ribonucleic acid (mRNA) COVID-19 vaccine.
- After extensive investigation, conclusive evidence identified the fatal diagnosis of sporadic Creutzfeldt-Jakob disease.

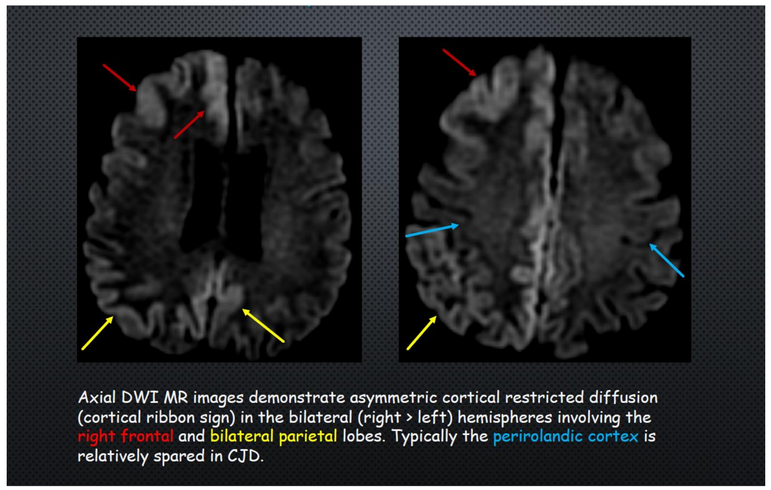
Introduction

Human prion diseases were first described in the early 1920s and are delineated into three categories: sporadic, inherited, or acquired by way of infection. Of the sporadic type, there are Creutzfeldt-Jakob disease (CJD), fatal insomnia, and variably protease-sensitive prionopathy. Approximately 90% of cases of prion disease are sporadic CJD, which can be further divided into five subtypes based on clinical features, histological findings on autopsy, and molecular structure of the abnormal protein [1]. The incidence of sCJD is very rare, approximately 1-2 cases per one million per population. In the case presented herein, the plausibility of the Pfizer-BioNTech COVID-19 vaccine triggering sCJD is explored.

Case

- A 64-year-old woman with a past medical history of bipolar depression and anxiety presents with rapidly progressive dementia, behavioral changes, headaches, and gait disturbance approximately one week after receiving the second dose of the Pfizer-BioNTech COVID-19 vaccine.
- Physical exam was essentially unremarkable except for confusion and significant distress regarding her condition.
- Initial labs, toxicology screening, and imaging were unremarkable except for a mildly increased white blood cell count.
- Psychiatry and neurology were consulted.
- Magnetic resonance (MR) imaging of the brain showed cortical diffusion restriction involving the bilateral frontal lobes, bilateral parietal lobes, and paramedian bilateral occipital lobes.
- Lumbar puncture: positive via the newest, highly sensitive real-time quaking-induced conversion (RT-QuIC) testing.
- T-tau protein measured at 38,979 (reference < 0-1,149).
- 14-3-3 protein was positive, neuron-specific enolase resulted at 16.3 (reference < 8.9).
- Exhibiting progressively worsening pyramidal and extrapyramidal symptoms, as well as akinetic mutism.
- Based on the Center for Disease Control and Prevention's diagnostic criteria, the findings place her case as probable sporadic CJD with a definitive diagnosis to be made by a proper autopsy with neuropathological studies.

Imaging



Axial DWI MR images demonstrate asymmetric cortical restricted diffusion (cortical ribbon sign) in the bilateral (right > left) hemispheres involving the right frontal and bilateral parietal lobes. Typically the perirolandic cortex is relatively spared in CJD.

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Discussion

- Normal prion protein is converted into an infectious, auto-enzymatic protein that aggregates in the brain tissue destroying neuronal cells leading to extensive neurodegeneration.
- Human prion protein (PrP), is encoded by the PrP gene, PRNP, which is located on the short arm of chromosome 20.
- Conversion to the diseased prion protein, termed PrPSc, is determined by PRNP polymorphism involving methionine (Met) or valine (Val) at codon 129 and prion strain (type 1 PrPSc or type 2 PrPSc).
- Etiology has been thought to be a mostly sporadic disease with no known specific cause.
- Retrospective case-control study in the United Kingdom found that all sporadic Creutzfeldt-Jakob disease (sCJD) cases from 1990 - 1998 lived close together, suggesting plausible precipitating factor.
- mRNA contained in the Pfizer-BioNTech COVID-19 vaccine has the potential to bind to specific proteins and cause pathologic misfolding.
- Various portions of the COVID-19 mRNA Pfizer-BioNTech vaccine to have a high affinity for cytoplasmic proteins such as TAR DNA binding proteins (TDP-43) and Fused in Sarcoma (FUS) .
- Spike protein, which is translated by the mRNA, can increase intracellular zinc, which has been shown to cause the conversion of TDP-43 into its pathological prion.
- Kuo et.al demonstrated how TDP-43 binds to mRNA transcripts with long UG-repeats.
- Pfizer-BioNTech's COVID-19 vaccine contains many of these specific sequences.
- Tetz and Tetz identified a prion-like domain found in the receptor-binding domain of the S1 region of the SARS-CoV-2 spike protein.
- A case reported a previously healthy 60-year-old man who developed sudden onset sCJD with concurrent onset of symptoms of COVID-19.
- Case of a patient with sCJD whom also had positive serum neuronal antibodies to the voltage-gated potassium channel complex (VGKC complex) and glycine receptor (GlyR) antibodies, suggesting a possible auto-immune mechanism.

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